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BY

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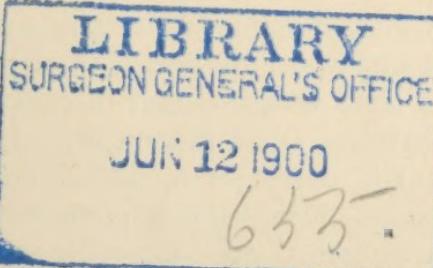
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SOME EXPERIMENTAL INVESTIGATIONS AS TO
THE EFFECTS OF THE ADMINISTRATION OF
YEAST NUCLEIN UPON THE LEUCOCYTES.

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THESE experiments were begun more than two years ago with the approval of Dr. Victor C. Vaughan and carried on at his desire. When the work was first conceived it was hoped that the investigations might be carried out to very complete and far-reaching results; but a change of teaching work in the last year made it impossible for me to carry on the experiments according to the first plan, and I have therefore found myself unable to complete the work. Nevertheless, in spite of this incompleteness, I think that the observations made have sufficient value to warrant their publication, and I am, moreover, unwilling to lose a year's labor, which was by no means small. The observations themselves establish certain points and bring the work to a position from which others may proceed with advantage.

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The various questions concerning nuclein, leucocytosis, and uric acid have during the last two years attracted so much attention that there is already an extensive literature upon the subject. It seems to me inexpedient in this paper to make a critical survey of this literature. The majority of the writers upon the subject assert that nuclein produces a leucocytosis, whether taken by the mouth or by injection. Horbaczewski emphasizes the relation of nuclein to leucocytosis and of the leucocytosis to an increased production of uric acid, and has formulated the theory that uric acid is formed from a nuclein produced by the leucocytes as one of the end products of their metabolism. By feeding nuclein to men and animals he demonstrated an increase of the uric acid eliminated, and since after a rich meat diet there is a temporary leucocytosis and a corresponding increase of the uric acid, he believes that the leucocytosis is produced by the nucleins of the food, and from the breaking down of an increased number of leucocytes comes the increase of uric acid.

It was the clearing up of these points, so far as yeast nuclein is concerned, that formed the object of these experiments. Dr. Vaughan had already demonstrated that leucocytosis could be produced in guinea-pigs by the injection of nuclein manufactured from yeast according to the method of his own. These experiments were carried on by Dr. Huber of the histological laboratory of this university. But Carter * in two animal experiments found that this same nuclein produced no leucocytosis. So far as I have been able to discover, these are the only experiments on record in

* *University Med. Mag.*, October, 1894.

which investigations as to the relation between yeast nuclein and the production of leucocytosis had been carried on, and from these cases my own experiments took departure. (See note.)

Numerous investigations have been made with brain, spleen, thyreoid, thymus, etc., nucleins, and in the majority of these it has been stated that a leucocytosis is usually produced by the administration of these substances. A survey of the records of these investigations leads me to the opinion that they are worthless so far as any exact knowledge of the condition of the leucocytes is concerned. Any conclusion based upon one estimation of the leucocytes daily is liable to complete error. That the daily variation of the number of leucocytes in the blood of normal persons is very great is a well-known fact to any one who has made many blood counts. To count the leucocytes in a patient on one day and find the number to be five thousand, and to find the count a week later to be eleven thousand, does not at all indicate the existence of a leucocytosis in that individual. The patient's daily range of leucocytes must be known before any conclusions can be drawn as to abnormalities in his count. I have found that the normal individual variations are very great. One subject may have a daily range of five thousand to eight thousand, and never go below or above these limits; another's range may be eight thousand to fourteen thousand; another's six thousand to fifteen thousand; yet all of these subjects may be apparently of equal health and practically under the same environment. Especially does the occurrence of leucocytosis after meals differ with the individual; some never have any increase at this time, in others it may be more than double the lowest count.

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made during the day. Therefore, I repeat that conclusions which are not based upon the individual's leucocyte range rather than upon isolated counts may be very misleading, and for this reason much of the work that has been done in this line is wholly unsatisfactory.

These investigations were begun with three points in view: The determination of the effect of nuclein taken into the body by injection or by the mouth upon the number of the leucocytes; the changes in the white corpuscles, and the relation of the amount of uric acid excreted to the nuclein injection and to the number of leucocytes. I soon found that the mere act of blood counting so frequently repeated took up all of the time that I could give to the work, and I was on that account forced to abandon the uric-acid estimations and confine myself to the first two questions.

It was thought best to make these experiments upon man rather than upon animals, and the experimental nature of the treatment was made clear to the normal individuals and to the hospital patients who consented to be made the subjects of the investigation. These individuals with the exception of two out-patients were placed under practically the same conditions of environment and nutrition. All other drugs were withheld during the period of observation. The patient's leucocyte range was first obtained by systematic counts made for several days (three to seven) before beginning the administration of the nuclein. These counts were made in definite time-relation to the taking of food, so that the counts would include the lowest and highest limits of the range. In the majority of the cases this was four times daily—an hour and a half after breakfast, just before dinner, an hour and a half after dinner, and

just before supper; but in many of the cases the counts were made hourly from 8 A. M. to 7 P. M., the approximate hour being given.

The counts were made with the Thoma-Zeiss counter, using both the red-corpuscle pipette and the one for the leucocytes. Toison's fluid was used as a diluent for the red-corpuscle pipette, and a one-third-per-cent. solution of acetic acid used in the white-corpuscle pipette. Four entire fields were counted from each pipette. If the counts from the two drops did not vary greatly, an average was made of the two results; if there was any great discrepancy the count was repeated. The liability to error was therefore much lessened. When several patients were counted on the same day the blood was taken as nearly as possible at the same time and the approximate time given.

The specimens for microscopic examination were prepared by spreading the covers, drying in the air, and hardening in equal parts of ether and absolute alcohol. They were then stained with eosin and haematoxylin. The differential count was then made by counting a thousand leucocytes, and from this count the numerical proportion of the various forms was estimated.

The temperature of the patient was always taken at the time of the count, and the symptoms arising from the injection were carefully noted.

The nuclein solution used was that prepared by Parke, Davis, & Co. from yeast, according to the method of Dr. Vaughan, and was stated to be a one-per-cent. solution in a 0.26 per cent. KOH and a 0.6 per cent. NaCl solution. The injections were given with a large-barrel syringe having a long needle. This was plunged deep into the gluteals, the injection never being given

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subcutaneously, it having been found by experience that this method gave much less pain to the patient. It is perhaps needless to say that strict antisepsis was carried out in the giving of the injection, and in the many hundreds of injections given only two abscesses occurred; and these from their nature seemed to be local necroses uninjected, as the bacteriological examination in both cases was negative.

Since it has been shown by Löwit and others that injections of weak solutions of many substances, including the alkalies, produce leucocytosis, and since the nuclein solution contained KOH in the strength of a 0.26-per-cent. solution and NaCl in the strength of a 0.6-per-cent. solution, it was also planned to control the experiments of the nuclein solution by giving injections of pure solutions of KOH and NaCl of the same strength as the percentage of these substances contained in the nuclein preparation.

CASE I.—L. S., a farmer boy of nineteen years, entered the hospital complaining of symptoms referred to sexual organs. The patient was well developed and well nourished, and the physical examination was entirely negative. Haemoglobin, 100; red corpuscles, 5,280,000; leucocytes, 8,000.

The patient was placed upon house diet, and all drugs withheld. The leucocytes were counted for several days, the counts being made four times daily at the same hours and in the same time relation to the taking of meals. For the three days previous to the beginning of the injections the counts were practically the same, as follows:

October 24, 1894.—8.30 A. M., leucocytes, 8,750. 11 A. M., leucocytes, 8,750. 1.30 P. M., leucocytes, 12,124. 4 P. M., leucocytes, 7,500.

The first injection was given on October 25, 1894.

At 8.30 A. M., one hour after breakfast, his leucocytes numbered 11,875. At 11 A. M. they were again counted, and found to be 7,916. Immediately after this count eight cubic centimetres of a one-per-cent. solution of the nuclein mentioned above were injected into the right gluteal region under strict antisepsis. At twelve o'clock the patient complained of faintness and ate no dinner. At 1 P. M. the leucocyte count was 14,636. During the afternoon he complained much of weakness, nausea, and pain in bones. Around the point of injection there was a dull red flush covering an area of about the size of a hand. This area was elevated, hard, and very sensitive.

At 3.30 P. M., the leucocytes were 29,686. The patient's temperature had risen very gradually after the injection, at four o'clock reaching 100.8°. After this time it fell, and patient felt much better. At 4.30 his leucocytes were 24,688.

On the next morning the patient still complained of nausea and general ill-feeling. At 9.30 A. M., two hours after breakfast, the leucocyte count was 18,175. Temperature at this time was 99.6° F. The point of injection was still red and tender. At 10 A. M. twelve cubic centimetres of the nuclein were injected into the left gluteal. The leucocytes were counted again at eleven o'clock, and found to be 19,219. His temperature had risen to 100.2° F., but patient said that he was feeling much better. A hearty dinner was eaten. At 1 o'clock his temperature had risen to 100.4° F., and the patient complained of much pain at the seat of injection. There was but little redness or swelling at this point. The leucocyte count was 23,750.

At 2 P. M. the patient had a severe chill; his temperature rose to 101° F., and he had frequent attacks of nausea and vomiting. The leucocyte count was 22,600.

At 3 P. M. the leucocytes were 26,256. The patient was still very ill with nausea, headache, chilliness, and pain in bones. His temperature was 103° F. This

rose to 104.2° F. at 4 P. M., when patient felt much better. The leucocytes at this time were 30,937.

On the next morning (October 27, 1894) at 8.30 the leucocytes were 30,833. He had eaten no supper the evening before, and had taken but little breakfast. He felt much better, but was still nauseated, and complained of soreness in muscles. Twelve cubic centimetres of the nuclein were injected into the right gluteal immediately after this count. 11 A. M., temperature 99.8°. The patient complained of nothing except slight pain at the point of injection. This was red, hard, and sensitive. Leucocytes, 20,891. 2 P. M., the patient complained of chilliness, nausea, and soreness in muscles. He vomited his dinner and had a slight attack of nosebleed. Temperature, 102.2°; leucocytes, 33,125. 4 P. M., temperature, 104°. Had slight chill, and vomited several times. Leucocytes, 30,813.

October 28th.—9 A. M., temperature, 100.2° F. The patient felt well with the exception of slight attacks of nausea. He could not retain his breakfast. Leucocytes, 20,000. 9.30 A. M., fourteen cubic centimetres of the nuclein solution were injected into the left gluteal. 11.30 A. M., temperature, 100.4°. Frequent attacks of nausea and vomiting. Leucocytes, 27,187. 7 P. M., temperature, 103.4°. The patient complained of feeling very faint. Leucocytes, 39,218.

October 29th.—10 A. M., the patient felt well and ate a hearty breakfast. Leucocytes, 22,975. No nuclein was injected on this day. 2 P. M., temperature, 100° F. Felt well. Leucocytes, 21,795. 7.30 P. M., temperature, 99.8°. Had slight headache. Leucocytes, 22,200. The region of the injections was still red and sensitive.

October 30th.—8.30 A. M., temperature, 98.6° F. Felt quite well. Leucocytes, 10,833. 11 A. M., temperature, 98.6°; leucocytes, 11,250. No injection. 3 P. M., temperature, 98.6°; leucocytes, 13,332. 7.30 P. M., temperature, 98.6°; leucocytes, 12,250.

October 31st.—8.30 A. M., temperature, 98.8° F.; leucocytes, 15,625. 11 A. M., temperature, 98.6°; leuco-

cytes, 16,250. No injection. 2 P. M., temperature, 98.8°; leucocytes, 15,206. 5 P. M., temperature, 98.8°; leucocytes, 12,703.

November 1st.—11 A. M., temperature, 98.8° F. No injection. Leucocytes, 11,875. 4.30 P. M., temperature, 98.8° F.; leucocytes, 11,250.

November 2d.—9 A. M., temperature, 98.8° F.; leucocytes, 9,062. No injection. 4.30 P. M., temperature, 98.8°; leucocytes, 8,500. The patient was discharged on this day. All symptoms arising from the injections had ceased, and patient claimed to feel better than before the injections were begun. There was still slight induration at the point of injections, but the redness had disappeared, and there was no pain.

CASE II.—Mr. T., merchant, aged forty-five years. The patient was of heavy build, but had small amount of fat and was of sallow color. He was under treatment for nervous dyspepsia; his physical examination was negative. Haemoglobin, 90; red corpuscles, 4,800,000; leucocytes, 6,250. The white cells were counted for a day and a half before beginning the injections.

October 30, 1894.—3.30 P. M., leucocytes, 6,250. 7 P. M., leucocytes, 10,000.

October 31st.—9 A. M., leucocytes, 7,875. 11.30 A. M., leucocytes, 5,832. 2.30 P. M., leucocytes, 8,332. 5.30 P. M., leucocytes, 7,187.

November 1st.—8.30 A. M., temperature, 98° F.; leucocytes, 7,708. 2 P. M., temperature, 98°; leucocytes, 6,505. Immediately after this count one cubic centimetre of nuclein was injected into the right gluteal. 2.05 P. M., temperature, 98°; leucocytes, 8,125. 2.15 P. M., temperature, 98°; leucocytes, 9,375. 2.30 P. M., temperature, 98°; leucocytes, 10,000. 3 P. M., temperature, 98.6°; leucocytes, 13,000. 4 P. M., temperature, 98.8°; leucocytes, 10,000. No symptoms. 5 P. M., temperature, 99°; leucocytes, 6,456.

November 2d.—8.45 A. M., temperature, 99° F.; leucocytes, 8,537. 11 A. M., temperature, 99.2°; leucocytes, 8,956. Two cubic centimetres of the nuclein were

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injected into the left gluteal immediately after this count. The patient complained of much pain at the seat of first injection. This was indurated, very sensitive, and slightly reddened. 11.05 A. M., temperature, 99.2°; leucocytes, 10,616. 1.45 P. M., temperature, 99.2°; leucocytes, 8,353. 3 P. M., temperature, 99.6°; leucocytes, 8,437. 5 P. M., temperature, 100.2°; leucocytes, 9,375. 7.45 P. M., temperature, 100.4°; leucocytes, 10,939. The symptoms resulting from the injection were slight, with the exception of the local pain. Occasional chilly sensations were the only things remarked by the patient.

November 3d.—8.45 A. M., temperature, 99° F.; leucocytes, 16,250. 11.15 A. M., temperature, 98°; leucocytes, 16,456. The patient did not feel so well this morning, but complained of pain in the muscles. Three cubic centimetres of nuclein were injected into the right gluteal after this count. 11.20 A. M., temperature, 98°; leucocytes, 14,321. 11.35 A. M., temperature, 98°; leucocytes, 12,625. 1.45 P. M., temperature, 98°; leucocytes, 10,308. 3 P. M., temperature, 98°; leucocytes, 8,750.

November 4th.—8.45 A. M., temperature, 98.6° F.; leucocytes, 11,406. 9 A. M., temperature, 98.6°; leucocytes, 11,406. Four cubic centimetres of nuclein were injected into the left gluteal after this count. There was no local reaction at point of previous injections, and patient said that he felt well. 9.05 A. M., temperature, 98.6°; leucocytes, 8,437. 10.30 A. M., temperature, 98.6°; leucocytes, 7,594. 2 P. M., temperature, 99.8°; leucocytes, 15,625. 4 P. M., temperature, 99.8°; leucocytes, 10,313. Slight nausea was complained of during the afternoon. No reaction at point of injection.

November 5th.—The patient felt well this morning and went for a walk, so the count was not taken up until afternoon. 1.30 P. M., temperature, 98.6° F.; leucocytes, 11,256. Six cubic centimetres of nuclein were injected into the right gluteal after this count. There was slight induration at the seat of the previous injections, other-

wise no reaction. 1.35 P. M., temperature, 98.6°; leucocytes, 12,625. 2 P. M., temperature, 98.6°; leucocytes, 8,333. 3.30 P. M., temperature, 98.6°; leucocytes, 9,894. 4 P. M., temperature, 98.6°; leucocytes, 8,019. 4.30 P. M., temperature, 99.8°; leucocytes, 11,894. 6 P. M., temperature, 99.8°; leucocytes, 11,719. 7.30 P. M., temperature, 101°; leucocytes, 11,563. He had slight chill during the evening, with headache and nausea.

November 6th.—The patient did not rest well during the night, but complained of fever and pain in bones. 9 A. M., temperature, 102° F.; leucocytes, 13,750. 10 A. M., temperature, 102°; leucocytes, 12,786. Immediately after this count twelve cubic centimetres of nuclein were injected into the left gluteal. The seat of yesterday's injection was red and swollen. 11 A. M., temperature, 102°; leucocytes, 15,626. 1.30 P. M., temperature, 102°; leucocytes, 16,637. 2.30 P. M., temperature, 102°; leucocytes, 15,208. Headache, nausea, pain in bones, dizziness, and chill. 4 P. M., temperature, 101.8°; leucocytes, 10,625. 5 P. M., temperature, 101.4°; leucocytes, 10,871. The patient was ill all day, but became better as the temperature fell.

November 7th.—9 A. M., temperature, 101.1° F.; leucocytes, 15,719. 11 A. M., temperature, 100°; leucocytes, 17,929. The patient declined to receive any more injections or to permit the continuation of the blood counts. Since the last injection of twelve cubic centimetres he had had intense headache, nausea, and muscular pain. The gluteal region was indurated, very red, and painful. He remained under observation for several days: the general symptoms disappeared with the subsidence of the local reaction.

CASE III.—Miss T., eighteen years of age, was referred from surgical clinic for nuclein treatment. She had been in the hospital for some time for tuberculosis of the right femur. The patient was pale, thin, but had no fever. She had a constant leucocytosis of 15,000 to 27,000. The haemoglobin was 70; the red blood-corpuscles were 3,000,000. The leucocytes were

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counted four times daily for three days before beginning the injections.

November 8, 1894.—8 A. M., temperature, 98.6° F.; leucocytes, 18,000. 10.30 A. M., temperature, 98.6°; leucocytes, 18,125. 2.30 P. M., temperature, 98.6°; leucocytes, 16,038. 5 P. M., temperature, 98.6°; leucocytes, 19,375.

November 9th.—8.30 A. M., temperature, 98.6° F.; leucocytes, 17,912. 12 noon, temperature, 98.6°; leucocytes, 27,500. 2 P. M., temperature, 98.6°; leucocytes, 25,000. 5 P. M., temperature, 98.6°; leucocytes, 20,966.

November 10th.—8.45 A. M., temperature, 98.6° F.; leucocytes, 15,104. 11.45 A. M., temperature, 98.6°; leucocytes, 18,509. 2.05 P. M., temperature, 98.8°; leucocytes, 17,963. 5 P. M., temperature, 98.8°; leucocytes, 14,375.

November 12th.—10 A. M., temperature, 99.2° F.; leucocytes, 16,250. After this count eight cubic centimetres of the nuclein were injected into the right glutæal. 10.10 A. M., temperature, 99.2°; leucocytes, 13,956. 10.30 A. M., temperature, 99.2°; leucocytes, 12,187. 11 A. M., temperature, 99.2°; leucocytes, 14,162. 12 noon, temperature, 99.6°; leucocytes, 14,000. 1 P. M., temperature, 99.6°; leucocytes, 14,162. 2 P. M., temperature, 99.6°; leucocytes, 14,064. 3.30 P. M., temperature, 100°; leucocytes, 16,061. No symptoms. 4.30 P. M., temperature, 100.4°; leucocytes, 20,519. 5.30 P. M., temperature, 100.8°; leucocytes, 21,350.

November 13th.—9 A. M., temperature, 99.4° F.; leucocytes, 17,500. An injection of twelve cubic centimetres of the nuclein was given after this count. 9.15 A. M., temperature, 99°; leucocytes, 13,853. 10 A. M., temperature, 99.6°; leucocytes, 14,109. 1 P. M., temperature, 100.8°; leucocytes, 20,103. 3 P. M., temperature, 100.8°; leucocytes, 26,143. 5 P. M., temperature, 104°; leucocytes, 19,375. Chill, nausea, headache, pain in bones.

November 14th.—8.30 A. M., temperature, 100° F.;

leucocytes, 20,625. Sixteen cubic centimetres of nuclein injected after this count. 8.50 A. M., temperature, 100°; leucocytes, 16,968. 9 A. M., temperature, 100°; leucocytes, 16,666. 10 A. M., temperature, 100°; leucocytes, 12,603. 11 A. M., temperature, 100°; leucocytes, 17,603. 12 noon, temperature, 100.2°; leucocytes, 17,000. 2 P. M., temperature, 100.2°; leucocytes, 20,312. 3 P. M., temperature, 100.6°; leucocytes, 12,907. 4.30 P. M., temperature, 100.4°; leucocytes, 13,212. 6 P. M., temperature, 100.2°; leucocytes, 16,250.

November 15th.—10.30 A. M., temperature, 98.6° F., leucocytes, 15,315. Fourteen cubic centimetres of nuclein were injected after this count. 10.45 A. M., temperature, 98.6°; leucocytes, 13,540. 12 noon, temperature, 98.6°; leucocytes, 12,706. 1.30 P. M., temperature, 99°; leucocytes, 13,763. No reaction. 3 P. M., temperature, 99.5°; leucocytes, 11,250. 5 P. M., temperature, 99.5°; leucocytes, 9,219.

November 16th.—Twelve cubic centimetres of nuclein injected at 9.30 A. M. The lowest count during the day was 12,000; the highest, 16,000. The patient had no reaction.

November 17th.—The reaction set in during the night with fever, sweating, and pain in bones. At 9 A. M. her temperature was 105°; the leucocytes at this time were 29,031. The point of injection was very red, hot, and painful. During the morning the patient had a severe chill. The fever continued all day; at 4 P. M. it was 104°. The leucocytes at this time were 31,250.

November 18th.—She had entirely recovered from the marked symptoms of yesterday, but the gluteal region was still very sensitive. Four cubic centimetres of nuclein were injected. No reaction during the day. The lowest count was 10,000; the highest, 14,687. For seven days four cubic centimetres of nuclein were injected daily. There was no reaction, local or general, and the leucocyte count during this time varied from 8,000 to 14,687. The injection of four cubic centimetres was continued daily until December 5th.

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There was no reaction and no change in the proportion of leucocytes. On this day the counts stood as follows: 8.45 A. M., temperature, 98.6° F.; leucocytes, 14,687. Four cubic centimetres of nuclein injected after this count. 9 A. M., temperature, 98.6°; leucocytes, 13,756. 10.45 A. M., temperature, 98.6°; leucocytes, 10,307. 2 P. M., temperature, 98.6°; leucocytes, 10,000. 4.30 P. M., temperature, 98.6°; leucocytes, 7,500. It was decided to operate upon the patient, so the treatment was discontinued.

December 7th.—The operation had been postponed, so the experiments were again taken up. With the consent of the patient it was decided to inject solutions of NaCl, NaOII, and KOII of the strength contained in the nuclein solution. 8.30 A. M., temperature, 98.6° F.; leucocytes, 9,688. Twelve cubic centimetres of a six-per-cent. solution of NaCl were injected into the right gluteal. 9.30 A. M., temperature, 98.6°; leucocytes, 10,206. 11 A. M., temperature, 98.6°; leucocytes, 12,300. 1.30 P. M., temperature, 98.6°; leucocytes, 12,300. 3.30 P. M., temperature, 98.8°; leucocytes, 15,000. 5 P. M., temperature, 98.8°; leucocytes, 11,875. The patient had no symptoms whatever.

December 8th.—8.45 A. M., temperature, 98.6° F.; leucocytes, 12,705. Twelve cubic centimetres of NaOII were injected after this count into the left gluteal. 10 A. M., temperature, 98.6°; leucocytes, 12,708. 11.30 A. M., temperature, 98.6°; leucocytes, 11,037. 3.30 P. M., temperature, 98.8°; leucocytes, 14,163. No symptoms.

December 9th.—8.45 A. M., temperature, 98.6° F.; leucocytes, 12,000. Twelve cubic centimetres of a 0.26-percent. solution of NaOII were injected into the right gluteal immediately after this count. 10 A. M., temperature, 98.6°; leucocytes, 12,708. 11.30 A. M., temperature, 98.6°; leucocytes, 14,000. 3.30 P. M., temperature, 98.8°; leucocytes, 14,000. The patient had no symptoms.

December 10th.—8.30 A. M., temperature, 98.6° F.;

leucocytes, 12,708. Twelve cubic centimetres of the 0.26-per-cent. solution of NaOH were injected after this count into the left gluteal. 10 A. M., temperature, 98.6°; leucocytes, 12,708. 11.30 A. M., temperature, 98.6; leucocytes, 11,078. 3.30 P. M., temperature, 98.8°; leucocytes, 13,000. The patient had no symptoms.

December 11th.—11 A. M., temperature, 98.6° F.; leucocytes, 10,675. Fourteen cubic centimetres of a 0.26-per-cent. solution of KOH injected into right gluteal after this count. 1 P. M., temperature, 98.6°; leucocytes, 11,875. 2.30 P. M., temperature, 98.6°; leucocytes, 13,282. 3.30 P. M., temperature, 98.8°; leucocytes, 14,375. 5.15 P. M., temperature, 98.8°; leucocytes, 10,000. There was no local reaction and patient had no symptoms.

December 12th.—8.30 A. M., temperature, 98.6° F.; leucocytes, 10,625. Sixteen cubic centimetres of the 0.26-per-cent. solution of KOH injected into the left gluteal. 1 P. M., temperature, 98.6°; leucocytes, 15,000. 3.30 P. M., temperature, 98.6°; leucocytes, 10,000. No local reaction; no symptoms save a slight diarrhoea.

December 13th.—10.30 A. M., temperature, 98.6° F.; leucocytes, 16,563. Sixteen cubic centimetres of the 0.26-per-cent. solution of KOH injected into the right gluteal. 11 A. M., temperature, 98.6°; leucocytes, 10,313. 2.30 P. M., temperature, 98.6°; leucocytes, 13,750. 4.30 P. M., temperature, 98.6°; leucocytes, 17,750. No local reaction; no symptoms; diarrhoea had ceased.

December 14th.—10 A. M., temperature, 98.6° F.; leucocytes, 11,094. Fourteen cubic centimetres of the 0.26-per-cent. solution of KOH injected after this count. 11.30 A. M., temperature, 98.6°; leucocytes, 10,937. A second injection of fourteen cubic centimetres of the 0.26-per-cent. solution of KOH injected into the right gluteal. 2 P. M., temperature, 98.8°; leucocytes, 11,250. 3.30 P. M., temperature, 100.6°; leucocytes, 11,875. 5 P. M., temperature, 100.6°; leucocytes, 15,625. The patient had slight nausea, headache, and

muscular pain. There was a red flush about the points of injections. An area of the size of a hand was indurated and very sensitive.

December 15th.—9 A. M., temperature, 98.6° F.; leucocytes, 11,250. The reaction of yesterday lasted but a few hours. It was decided to return to the nuclein injections. Fourteen cubic centimetres of the nuclein solution injected into the left gluteal. 3 P. M., temperature, 98.6°; leucocytes, 15,000. 5 P. M., temperature, 98.6°; leucocytes, 12,500. There was no reaction, local or general.

December 16th.—9 A. M., temperature, 98.6° F.; leucocytes, 15,000. At 9.30 fourteen cubic centimetres of the nuclein solution were injected into the right gluteal. 11.30 A. M., temperature, 98.6°; leucocytes, 15,000. 3.30 P. M., temperature, 98.6°; leucocytes, 14,500. There was a slight general reaction, nausea, etc.

December 17th.—9 A. M., temperature, 98.6° F.; leucocytes, 10,000. Twelve cubic centimetres of the nuclein solution injected into the left gluteal after this count. 11 A. M., temperature, 98.6°; leucocytes, 9,500. 5 P. M., temperature, 98.6°; leucocytes, 10,000. There was no reaction.

December 18th.—9.45 A. M., temperature, 98.6° F.; leucocytes, 11,875. Twelve cubic centimetres of the nuclein solution injected into the right gluteal. 10 A. M., temperature, 98.6°; leucocytes, 10,000. 11 A. M., temperature, 98.6°; leucocytes, 10,150. 1.30 P. M., temperature, 98.6°; leucocytes, 13,250. 3.30 P. M., temperature, 98.8°; leucocytes, 15,000. 5.50 P. M., temperature, 98.8°; leucocytes, 16,250. There was no reaction, local or general.

December 19th.—8.30 A. M., temperature, 98.6° F.; leucocytes, 14,300. Twelve cubic centimetres of the nuclein solution injected into the left gluteal. 11.30 A. M., temperature, 98.6°; leucocytes, 10,000. 2 P. M., temperature, 98.6°; leucocytes, 16,275. 5 P. M., temperature, 98.6°; leucocytes, 15,000. There was no reaction, local or general.

December 20th.—8.45 A. M., temperature, 98.6° F.; leucocytes, 14,375. Fourteen cubic centimetres of the nuclein solution injected into the right gluteal. 11 A. M., temperature, 98.6°; leucocytes, 10,000. 2 P. M., temperature, 98.6°; leucocytes, 14,375. 5 P. M., temperature, 98.6°; leucocytes, 15,000. There was no reaction, local or general.

December 21st.—8.30 A. M., temperature, 98.6° F.; leucocytes, 13,000. Fourteen cubic centimetres of the nuclein solution injected into the right gluteal. 11 A. M., temperature, 98.6°; leucocytes, 10,000. 2 P. M., temperature, 98.6°; leucocytes, 15,000. 5 P. M., temperature, 98.6°; leucocytes, 16,375. There was no reaction, local or general.

December 22d.—8.45 A. M., temperature, 99.8° F.; leucocytes, 14,375. 9.30 A. M., temperature, 99.8°; leucocytes, 16,250. Eight cubic centimetres of the nuclein solution injected into the left gluteal. The right gluteal region is very red, hard, and painful. 9.45 A. M., temperature, 99.8°; leucocytes, 16,250. 11.30 A. M., temperature, 100.2°; leucocytes, 18,125. 2 P. M., temperature, 102°; leucocytes, 11,875. 4 P. M., temperature, 100.2°; leucocytes, 18,750. 5 P. M., temperature, 100°; leucocytes, 15,000. The patient felt very ill all day; severe headache, nausea, and pain in muscles.

December 23d.—The patient was ill all night. Gluteals so red and swollen that it was thought best to stop the injections. Temperature rose from 100° to 104° F.; leucocytes, 18,000 to 20,000.

Since yesterday symptoms continued with increase of the local condition. Fluctuation was obtained at the seat of the two injections of KOH made on the 14th into the right gluteal. An incision was made and eight drachms of what seemed to be entirely liquid fat mixed with a small quantity of blood were removed. Under the microscope this was found to consist chiefly of fat droplets, a moderate number of pus cells, and blood-corpuscles. A bacteriological examination was

negative (?). The temperature varied from 101° to 102°; the leucocytes remained at 18,750.

The patient was observed for some time longer; the abscess soon healed; temperature became normal, and the daily average of leucocytes was 12,000. In spite of the discomfort arising from the abscess the patient made constant improvement during the period of injections. The nuclein was withheld eight days, and then the internal administration was begun. Five cubic centimetres were given three times daily for six weeks. During this time no reaction was ever obtained, hence systematic counts of the leucocytes were not made.

CASE IV.—Miss M. The patient was twenty years of age, slight frame, anaemic and emaciated. She was under treatment in the surgical clinic for bone tuberculosis, and was referred for nuclein treatment. Haemoglobin, 50; red corpuscles, 2,500,000. There was a constant leucocytosis of 18,000 to 25,000.

Four cubic centimetres of the nuclein solution were injected daily for five weeks. There was never any reaction, and the daily range of the leucocyte count was not materially affected.

CASE V.—Mrs. C. This patient, thirty-five years of age, had extensive tuberculous infiltration in both upper lobes. Her haemoglobin was 85, red blood-corpuscles were 4,000,000, and the daily average of leucocytes was 7,500. Four cubic centimetres of the nuclein solution were injected daily for six weeks. There was never any reaction, and the daily average of leucocytes was practically unchanged. The patient declined rapidly during the treatment.

CASE VI.—Mr. J., a farm boy, eighteen years of age, had tuberculosis in upper right lobe. The patient was in good condition. Haemoglobin, 100; red blood-corpuscles, 5,000,000; leucocytes, 8,000 to 10,000. Four cubic centimetres of the nuclein solution were injected daily for two months. The patient did not remain in the hospital during this period, so that temperature observations could not be taken, but he had no symptoms

of the usual reaction, and his leucocytes, taken at frequent intervals, showed no disturbance. The patient made distinct improvement while under this treatment, but was lost sight of later. (Is now working, and said to be entirely free from symptoms.—Dr. Dock.)

CASE VII.—Mr. S., referred from surgical clinic for nuclein treatment because of bone tuberculosis. The patient's age was forty; he was much emaciated and weak. Hæmoglobin, 70; red blood-corpuscles, 4,000,000; leucocytes, 7,000 to 8,000. Four cubic centimetres of the nuclein solution were injected daily for one month. There was never any reaction, and the leucocyte count was practically unchanged.

CASE VIII.—Mr. R., aged forty, referred from surgical clinic for nuclein treatment because of tuberculosis of the genito-urinary tract. The patient was in good condition; hæmoglobin, 100; red blood-corpuscles, 4,500,000. The daily average of leucocytes was 7,500. Four cubic centimetres of the nuclein solution were injected for two months. There was never any reaction, and the leucocyte count was unchanged. The patient improved under the treatment.

CASE IX.—Miss D., twenty-six years of age, had tuberculosis of cervical glands. These were removed by Dr. Nancrede, and the patient was referred for treatment with nuclein. The patient was in fair condition. Hæmoglobin, 90; red blood-corpuscles, 4,500,000; the leucocytes ranged from 6,000 to 10,000. Five cubic centimetres of the nuclein solution were injected daily from February 5th to March 3d. There was never any reaction, and the leucocyte range remained exactly as before, the lowest daily count being 6,000, and the highest, one hour after meals, being 10,000. The patient gained rapidly during this month.

CASE X.—Mr. S., laborer, aged forty-five, had extensive tuberculosis on both sides, with large cavity in upper right. He was very weak, much emaciated, and had daily temperature of 100° to 104° F. He had also daily chill, sweat, and profuse purulent expectoration.

Nevertheless there was no leucocytosis, the daily count ranging from 6,000 to 9,000. His haemoglobin was 70; red blood-corpuscles, 4,000,000. Five cubic centimetres of the nuclein solution were injected daily from February 15th to March 6th. His daily symptoms remained unchanged, and the highest count of leucocytes during this time was 9,878. The patient failed quickly, was sent home, and died soon after.

CASE XI.—Mr. A., pulmonary tuberculosis. The patient was in fair condition. Haemoglobin, 90; red blood-corpuscles, 4,500,000. He had daily range of leucocytes from 10,000 to 20,000. His temperature ran from 100° to 101° F. For three days previous to the beginning of the injections the daily average of leucocytes was 15,000. Five cubic centimetres of the nuclein solution were injected daily for six weeks. There was never any reaction that could be distinguished from the symptoms which he had had before the injections were begun. There was no increase of leucocytosis, the daily average varying but slightly from 15,000 to 16,000. The patient made no improvement during the period of the injections.

CASE XII.—Mr. A., a farmer, twenty-six years of age, had been under treatment in the clinic of dermatology for chronic furunculosis. He had also intermittent haematuria. His general condition was fair. Haemoglobin, 90; red blood-corpuscles, 4,500,000. There was a constant leucocytosis of 10,000 to 18,000, the daily average varying from 13,000 to 15,000. Six counts were made daily.

December 21, 1894.—No injection. Average, 13,271.
22d.—No injection. Average, 14,975.
23d.—No injection. Average, 13,493.
24th.—Nuclein, five cubic centimetres. Average, 17,031.

The patient had a slight reaction during the afternoon, when the leucocytes reached 19,000.

25th.—Nuclein, five cubic centimetres. Average, 12,341. No reaction.

26th.—Nuclein, five cubic centimetres.	Average,
15,619. Slight reaction.	
27th.—Nuclein, five cubic centimetres.	Average,
17,190. Slight reaction.	
28th.—Nuclein, five cubic centimetres.	Average,
12,081. No reaction.	
29th.—Nuclein, five cubic centimetres.	Average,
12,187. No reaction.	
30th.—Nuclein, five cubic centimetres.	Average,
14,219. No reaction.	
31st.—Nuclein, five cubic centimetres.	Average,
11,407. No reaction.	
<i>January 1, 1895.</i> —Nuclein, five cubic centimetres.	
Average, 12,000. No reaction.	
2d.—Nuclein, five cubic centimetres.	Average,
11,719. No reaction.	
3d.—Nuclein, five cubic centimetres.	Average,
12,960. No reaction.	
4th.—Nuclein, five cubic centimetres.	Average,
11,000. No reaction.	
5th.—Nuclein, five cubic centimetres.	Average,
12,000. No reaction.	

The injections were then stopped and the leucocytes counted for a week. The average remained at 11,000 to 12,000. The reaction on the 24th, 26th, and 27th was slight, but the point of injection in the gluteals was much reddened, indurated, and painful.

CASE XIII.—Mr. B., farmer, aged twenty-seven, sexual neurasthenic; of good nutrition. Hæmoglobin, 100; red blood-corpuscles, 5,000,000. The leucocyte count varied from six to eleven thousand.

January 23, 1895.—9.30 A. M., leucocytes, 9,375. 11.15 A. M., leucocytes, 9,375. 1.30 P. M., leucocytes, 10,000. 5 P. M., leucocytes, 11,750.

24th.—9.30 A. M., leucocytes, 8,750. 11 A. M., leucocytes, 9,750. 1.30 P. M., leucocytes, 10,000. 5.30 P. M., leucocytes, 10,250.

25th.—9.30 A. M., leucocytes, 8,750. Five cubic centimetres of a 0.26-per-cent. KOH solution injected

after this count. 11.30 A. M., leucocytes, 10,000. 1.30 P. M., leucocytes, 10,000. 5.30 P. M., leucocytes, 9,750. No reaction.

26th.—9.30 A. M., leucocytes, 8,750. Five cubic centimetres of the KOH solution injected after this count. 11.30 A. M., leucocytes, 11,000. 1.30 P. M., leucocytes, 9,000. 5.30 P. M., leucocytes, 10,000. No reaction.

27th.—9.30 A. M., leucocytes, 8,750. Five cubic centimetres of the KOH solution injected after this count. 11 A. M., leucocytes, 9,000. 1.30 P. M., leucocytes, 10,000. 5.30 P. M., leucocytes, 10,000. No reaction.

28th.—8.30 A. M., leucocytes, 8,000. Five cubic centimetres of the KOH solution injected after this count. 11.30 A. M., leucocytes, 8,750. 1.30 P. M., leucocytes, 10,000. 5.30 P. M., leucocytes, 10,000. No reaction.

29th.—8.30 A. M., leucocytes, 6,750. Five cubic centimetres of KOH. 11 A. M., leucocytes, 8,750. 1.30 P. M., leucocytes, 10,000. 5.30 P. M., leucocytes, 10,000. No reaction.

30th.—8.30 A. M., leucocytes, 8,750. Five cubic centimetres KOH. 11 A. M., leucocytes, 8,750. 1.30 P. M., leucocytes, 10,000. 5.30 P. M., leucocytes, 8,750. No reaction.

31st.—8.30 A. M., leucocytes, 8,750. Five cubic centimetres KOH. 11.30 A. M., leucocytes, 10,000. 1.30 P. M., leucocytes, 10,000. 5.30 P. M., leucocytes, 8,750. No reaction.

February 1st.—8.30 A. M., leucocytes, 8,750. Five cubic centimetres KOH. 11 A. M., leucocytes, 8,750. 1.30 P. M., leucocytes, 10,000. 5.30 P. M., leucocytes, 7,500. No reaction.

2d.—8.30 A. M., leucocytes, 6,750. Five cubic centimetres KOH. 11 A. M., leucocytes, 7,500. 1.30 P. M., leucocytes, 10,000. 5.30 P. M., leucocytes, 8,750. No reaction.

3d.—8.30 A. M., leucocytes, 10,000. Five cubic centimetres KOH. 10 A. M., temperature, 100.8° F.; leuco-

cytes, 12,500. Slight reaction. 1.30 p. m., temperature, 99.6°; leucocytes, 10,000. 5.30 p. m., temperature, 99.6°; leucocytes, 10,000.

4th.—8.30 a. m., leucocytes, 6,785. Five cubic centimetres KOH. 11.30 a. m., leucocytes, 7,850. 1.30 p. m., leucocytes, 8,750. 5.30 p. m., leucocytes, 8,765. No reaction.

5th.—8.30 a. m., leucocytes, 8,000. Five cubic centimetres KOH. 11 a. m., leucocytes, 7,865. 1.30 p. m., leucocytes, 8,765. 5.30 p. m., leucocytes, 10,000. No reaction.

6th.—8.30 a. m., Leucocytes, 7,865. Five cubic centimetres KOH. 11 a. m., leucocytes, 8,750. 1.30 p. m., leucocytes, 10,750. 5.30 p. m., leucocytes, 9,876. No reaction.

7th.—8.30 a. m., leucocytes, 7,865. Five cubic centimetres KOH. 11.30 a. m., leucocytes, 8,765. 1.30 p. m., leucocytes, 10,000. 3 p. m., leucocytes, 9,876. No reaction.

8th.—8.30 a. m., leucocytes, 6,875. Five cubic centimetres KOH. 11 a. m., leucocytes, 7,865. 1.30 p. m., leucocytes, 10,000. 5 p. m., leucocytes, 9,875. No reaction.

9th.—9 a. m., leucocytes, 7,650. Five cubic centimetres KOH. 11.30 a. m., leucocytes, 7,865. 1.30 p. m., leucocytes, 11,000. 5.30 p. m., leucocytes, 9,750. No reaction.

10th.—8.30 a. m., leucocytes, 6,875. Five cubic centimetres KOH. 11 a. m., leucocytes, 7,500. 1.30 p. m., leucocytes, 10,000. 5 p. m., leucocytes, 8,986. No reaction.

11th.—8.30 a. m., leucocytes, 8,760. Five cubic centimetres KOH. 11 a. m., leucocytes, 7,500. 1.30 p. m., leucocytes, 10,765. 5.30 p. m., leucocytes, 8,968. No reaction.

12th.—8.30 a. m., leucocytes, 8,765. Five cubic centimetres KOH. 11.30 a. m., leucocytes, 7,863. 1.30 p. m., leucocytes, 11,635. 5.30 p. m., leucocytes, 10,000. No reaction.

24 EFFECTS OF YEAST NUCLEIN ON LEUCOCYTES.

13th.—8.30 A. M., leucocytes, 6,785. Five cubic centimetres nuclein solution. 11.30 A. M., leucocytes, 7,867. 1.30 P. M., leucocytes, 9,879. 5 P. M., leucocytes, 8,765. No reaction.

14th.—8.30 A. M., leucocytes, 8,750. Five cubic centimetres nuclein. 11.30 A. M., leucocytes, 9,876. 1.30 P. M., leucocytes, 10,000. 5.30 P. M., leucocytes, 8,750. No reaction.

15th.—8.30 A. M., leucocytes, 12,500. No reaction. Five cubic centimetres nuclein. 11.30 A. M., leucocytes, 8,765. 1.30 P. M., leucocytes, 9,879. 5.30 P. M., leucocytes, 8,750.

16th.—8.30 A. M., leucocytes, 8,576. Five cubic centimetres nuclein. 11 A. M., leucocytes, 8,750. 1.30 P. M., leucocytes, 11,000. 5.30 P. M., leucocytes, 8,750. No reaction.

17th.—8.30 A. M., leucocytes, 8,765. Five cubic centimetres nuclein. 11.30 A. M., leucocytes, 8,765. 1.30 P. M., leucocytes, 10,678. 5 P. M., leucocytes, 8,765. No reaction.

18th.—8.30 A. M., leucocytes, 8,768. Five cubic centimetres of nuclein. 11.30 A. M., leucocytes, 7,869. 1.30 P. M., leucocytes, 9,986. 5.30 P. M., leucocytes, 8,968. No reaction.

19th.—8.30 A. M., leucocytes, 7,850. Five cubic centimetres nuclein. 11 A. M., leucocytes, 8,768. 1.30 P. M., leucocytes, 10,000. 5.30 P. M., leucocytes, 9,896. No reaction.

The injection of five cubic centimetres of the nuclein solution was continued daily until March 6th. The blood counts were also kept up during this period. There was never any leucocytosis, the daily average running from 6,000 to 8,000. The patient had no symptoms whatever from the injections except on the one day noted. There was never any redness or swelling at place of injection. This patient also declared himself to be relieved of his sexual symptoms through the treatment, but the inference may be drawn that the benefit in these sexual cases came through suggestion.

CASE XIV.—Mr. B., aged twenty-six, farmer, was under treatment for muscular rheumatism. He was well nourished. Haemoglobin, 100; red blood-corpuscles, 5,000,000; leucocytes varied from 6,000 to 8,000. These were counted regularly for three days before beginning the injections. The count for the last of the days will serve, as it was almost exactly the same for the three days.

November 16, 1894.—8.30 A. M., temperature, 98.6° F.; leucocytes, 6,042. 11.30 A. M., temperature, 98.6°; leucocytes, 7,500. 1 P. M., temperature, 98.6°; leucocytes, 7,912. 3.30 P. M., temperature, 98.6°; leucocytes, 6,250. 5.30 P. M., temperature, 99°; leucocytes, 6,878.

November 17th.—8.30 A. M., temperature, 98.6° F.; leucocytes, 5,000. 11.30 A. M., temperature, 98.6°; leucocytes, 5,312. Nuclein, twelve cubic centimetres. 11.45 A. M., temperature, 98.6°; leucocytes, 7,500. 12 noon, temperature, 98.6°; leucocytes, 8,750. Slight chill. 1.30 P. M., temperature, 100°; leucocytes, 5,000. 2.30 P. M., temperature, 100°; leucocytes, 6,875. Strong reaction. 3.30 P. M., temperature, 102.8°; leucocytes, 14,063. Felt better. 6 P. M., temperature, 101.7°; leucocytes, 13,437. The reaction was that observed in all of the cases in which it occurred. The point of injection was flushed, indurated, and painful. The patient complained of nausea, chilliness, pain in bones, and great weakness; these symptoms being compared by the patient to those of *grippe*.

November 18th.—10.30 A. M., temperature, 98.6° F.; leucocytes, 10,213. Felt well. Sixteen cubic centimetres of nuclein injected. 10.35 A. M., temperature, 98.6°; leucocytes, 7,708. 10.45 A. M., temperature, 98.6°; leucocytes, 4,750. 12 noon, temperature, 98.6°; leucocytes, 9,650. 1.30 P. M., temperature, 100.8°; leucocytes, 13,331. 2.30 P. M., temperature, 101.4°; leucocytes, 14,791. Reaction. 4 P. M., temperature, 102.6°; leucocytes, 14,700. Very ill. 5 P. M., temperature, 102.8°; leucocytes, 15,630. Felt better. The symptoms of the reaction were the same as on the preceding day.

These symptoms will be covered by the term reaction hereafter.

November 19th.—8.30 A. M., temperature, 99.8° F.; leucocytes, 14,600. Sixteen cubic centimetres of nuclein injected. 8.45 A. M., temperature, 99.8°; leucocytes, 14,375. Felt ill. 10 A. M., temperature, 99.8°; leucocytes, 16,250. 11 A. M., temperature, 99.8°; leucocytes, 16,250. 1.30 P. M., temperature, 102.5°; leucocytes, 21,250. Strong reaction. 3 P. M., temperature, 102.6°; leucocytes, 19,000. 5 P. M., temperature, 102.6°; leucocytes, 19,000.

November 20th.—8.30 A. M., temperature, 100° F.; leucocytes, 13,853. 1.30 P. M., temperature, 100°; leucocytes, 10,700. 4 P. M., temperature, 100°; leucocytes, 10,630. The patient felt too ill to receive an injection. He felt quite well in the evening.

November 21st.—10.30 A. M., temperature, 98.6° F.; leucocytes, 8,751. Sixteen cubic centimetres of nuclein injected. 10.45 A. M., temperature, 98.6°; leucocytes, 8,750. 11.45 A. M., temperature, 98.6°; leucocytes, 9,032. 1.30 P. M., temperature, 100°; leucocytes, 13,125. 3.30 P. M., temperature, 100°; leucocytes, 15,312. Strong reaction. 5 P. M., temperature, 101°; leucocytes, 16,666. 7.30 P. M., temperature, 102°; leucocytes, 14,375.

November 22d.—8.30 A. M., temperature, 100° F.; leucocytes, 14,600. Ten cubic centimetres of nuclein injected. 9.15 A. M., temperature, 99.6°; leucocytes, 12,300. 10 A. M., temperature, 99.6°; leucocytes, 9,375. 11 A. M., temperature, 101.6°; leucocytes, 11,406. 2.30 P. M., temperature, 101.6°; leucocytes, 15,304. Reaction. 3.30 P. M., temperature, 101.6°; leucocytes, 13,750. 5.30 P. M., temperature, 101.2°; leucocytes, 15,562.

November 23d.—9 A. M., temperature, 99.6° F.; leucocytes, 15,000. Fifteen cubic centimetres of nuclein injected. 9.45 A. M., temperature, 99.6°; leucocytes, 10,413. 10 A. M., temperature, 99.6°; leucocytes, 10,000. 11.30 A. M., temperature, 99.6°; leucocytes, 14,375. 1.30 P. M., temperature, 101.6°; leucocytes, 20,206. Reaction. 3 P. M., temperature, 101.4°; leucocytes, 20,000. 5.30 P. M., temperature, 101.1°; leucocytes, 14,375.

November 24th.—9 A. M., temperature, 99.8° F.; leucocytes, 10,000. Fifteen cubic centimetres of nuclein injected. 10 A. M., temperature, 98.6°; leucocytes, 10,345. 11.30 A. M., temperature, 98.6°; leucocytes, 14,375. 1.30 P. M., temperature, 98.6°; leucocytes, 14,000. 3 P. M., temperature, 101.8°; leucocytes, 20,000. 5 P. M., temperature, 101.8°; leucocytes, 15,000.

During the next three days no nuclein was injected. All of the symptoms of the reaction had disappeared by the second day, and on the third day the leucocytes had returned to their former count as shown by the count on the 27th, when the lowest count was 6,800 and the highest was 8,000.

November 28th.—8.30 A. M., temperature, 98.6° F.; leucocytes, 8,000. Sixteen cubic centimetres of a 0.26 KOH and 0.6-per-cent. solution NaCl injected. 9 A. M., temperature, 98.6°; leucocytes, 8,537. 9.30 A. M., temperature, 98.6°; leucocytes, 6,666. 10 A. M., temperature, 98.6°; leucocytes, 6,785. 11 A. M., temperature, 98.6°; leucocytes, 6,785. 2 P. M., temperature, 98.6°; leucocytes, 11,652. 3 P. M., temperature, 98.6°; leucocytes, 15,206. 4 P. M., temperature, 98.6°; leucocytes, 12,500. 4.45 P. M., temperature, 98.6°; leucocytes, 10,500. The patient had no reaction, local or general.

November 29th.—8.45 A. M., temperature, 98.6° F.; leucocytes, 7,706. Sixteen cubic centimetres of 0.26-per-cent. KOH and 0.6-per-cent. NaCl injected. 10 A. M., temperature, 98.6°; leucocytes, 6,663. 10.15 A. M., temperature, 98.6°; leucocytes, 4,563. 10.30 A. M., temperature, 98.6°; leucocytes, 6,875. 2.45 P. M., temperature, 102°; leucocytes, 25,000. Reaction. 4 P. M., temperature, 102°; leucocytes, 18,235.

November 30th.—The patient had a very severe reaction during the night. Felt too ill to have blood counted. Temperature, 103°. Sixteen cubic centimetres of the KOH and NaCl solution injected.

December 1st.—9 A. M., temperature, 99.4° F.; leucocytes, 14,575. The patient had not recovered from the reaction of yesterday. Sixteen cubic centimetres of the KOH and NaCl solution injected. 10 A. M., tempera-

ture, 99.4°; leucocytes, 13,000. 10.30 A. M., temperature, 99.4°; leucocytes, 13,575. 11.15 A. M., temperature, 99.4°; leucocytes, 14,580. 2 P. M., temperature, 99.4°; leucocytes, 24,163. 3 P. M., temperature, 99.4°; leucocytes, 23,341. 6 P. M., temperature, 102°; leucocytes, 23,541. The patient had a very severe reaction, complaining of stiffness, numbness, headache, and nausea. The heart action was very weak, the sounds being very weak, and the rate was not increased in proportion to the temperature.

December 2d.—9 A. M., temperature, 100.2° F.; leucocytes, 27,288. Twelve cubic centimetres of a 0.26-per-cent. solution of KOH was injected. The patient was still under the effects of yesterday's injection, and felt very ill. 10 A. M., temperature, 100.2°; leucocytes, 24,787. 11 A. M., temperature, 100.2°; leucocytes, 25,-206. 2 P. M., temperature, 102.4°; leucocytes, 26,250. Hard chill. 4.45 P. M., temperature, 104°; leucocytes, 19,164. 7 P. M., temperature, 104°; leucocytes, 21,041. The reaction was very severe.

December 3d.—8.30 A. M., temperature, 99.6° F.; leucocytes, 22,187. Sixteen cubic centimetres of a 0.6-per-cent. solution of NaCl injected. 10 A. M., temperature, 99.6°; leucocytes, 21,875. 11.15 A. M., temperature, 99.6°; leucocytes, 20,000. 1.15 P. M., temperature, 99.6°; leucocytes, 20,000. 3.15 P. M., temperature, 99.6°; leucocytes, 14,686. 5 P. M., temperature, 100°; leucocytes, 23,427. The patient had no reaction.

December 4th.—8.30 A. M., temperature, 98.6° F.; leucocytes, 10,625. 11 A. M., temperature, 98.6°; leucocytes, 10,625. 1.30 P. M., temperature, 98.6°; leucocytes, 10,000. 5 P. M., temperature, 98.6°; leucocytes, 10,000. The patient received no injection on this day, and on the two days following there was none given. The leucocytes fell to their normal level, 6,000 to 8,000.

December 7th.—10 A. M., leucocytes, 8,750. Twelve cubic centimetres of a 0.26-per-cent. solution of NaOII injected. 10.30 A. M., temperature, 98.6° F.; leucocytes, 7,081. 11.45 A. M., temperature, 98.6°; leuco-

cytes, 7,283. 3.30 P. M., temperature, 98.6°; leucocytes, 11,563. The patient had no reaction.

December 8th.—8.30 A. M., leucocytes, 7,867. Twelve cubic centimetres of the 0.26-per-cent. NaOH solution injected. 11 A. M., temperature, 98.6° F.; leucocytes, 7,869. 1.30 P. M., temperature, 98.6°; leucocytes, 10,000. 5 P. M., temperature, 98.6°; leucocytes, 8,768. There was no reaction, local or general.

December 9th.—8.30 A. M., leucocytes, 8,000. Twelve cubic centimetres of the 0.26-per-cent. NaOH solution injected. 10 A. M., temperature, 98.6° F.; leucocytes, 6,000. 1.30 P. M., temperature, 98.6°; leucocytes, 7,765. 5 P. M., temperature, 98.6°; leucocytes, 8,000. There was no reaction.

December 10th.—8.30 A. M., temperature, 98.6° F.; leucocytes, 8,000. Twelve cubic centimetres of the 0.26-per-cent. solution of NaOH injected. 10.30 A. M., temperature, 98.6°; leucocytes, 6,786. 1.30 P. M., temperature, 98.6°; leucocytes, 8,000. 5 P. M., temperature, 98.6°; leucocytes, 7,867. The injection of the NaOH solution was continued two days. There was no reaction, and no change in the leucocyte range.

CASE XV.—Mr. K., a clerk, had pulmonary tuberculosis. The patient was emaciated, anaemic, and very weak. He had daily temperature variation from 100° to 101° F., rarely reaching 102° F.; he had also abundant purulent expectoration. His haemoglobin was 70, red blood-corpuscles were 4,000,000, and the daily range of leucocytes was from 6,000 to 13,000, an average of 9,000. Injections of the 0.26-per-cent. solution of KOH were begun on December 11th.

December 11, 1894.—10.30 A. M., temperature, 98.8° F.; leucocytes, 6,563. Twelve cubic centimetres of the KOH solution injected. 1 P. M., temperature, 98.8°; leucocytes, 12,187. 2.30 P. M., temperature, 98.8°; leucocytes, 11,250. 3.30 P. M., temperature, 99.8°; leucocytes, 11,875. Reaction. 5.30 P. M., temperature, 101.2°; leucocytes, 10,000. Chill.

December 12th.—8.30 A. M., temperature, 99.6° F.;

leucocytes, 12,500. Sixteen cubic centimetres of the KOH solution injected. 9.15 A. M., temperature, 99.6°; leucocytes, 7,000. 10.30 A. M., temperature, 99.6°; leucocytes, 12,300. 1.30 P. M., temperature, 100.4°; leucocytes, 15,625. Reaction. 3.30 P. M., temperature, 101°; leucocytes, 15,789. 5.30 P. M., temperature, 102°; leucocytes, 20,000. Chill.

December 13th.—8.30 A. M., temperature, 99.6° F.; leucocytes, 11,668. Sixteen cubic centimetres of the KOH solution injected. 9 A. M., temperature, 99.6°; leucocytes, 10,344. 10 A. M., temperature, 99.6°; leucocytes, 5,625. 11 A. M., temperature, 99.6°; leucocytes, 9,678. 2 P. M., temperature, 100.6°; leucocytes, 13,125. 4.15 P. M., temperature, 100.8°; leucocytes, 8,750. 5.30 P. M., temperature, 100.6°; leucocytes, 7,500. The patient had no chill, but late in the evening had nausea, headache, and pain in bones.

December 14th.—9.45 A. M., temperature, 99.6° F.; leucocytes, 8,750. Sixteen cubic centimetres of the KOH solution injected. 10.30 A. M., temperature, 99.6°; leucocytes, 8,750. 11.30 A. M., temperature, 99.6°; leucocytes, 8,750. 2 P. M., temperature, 100.6°; leucocytes, 11,563. 3.30 P. M., temperature, 100.6°; leucocytes, 15,000. Severe reaction. 5 P. M., temperature, 100.6°; leucocytes, 11,875. The patient had severe symptoms, but no chill or fever.

December 15th.—10.15 A. M., temperature, 98.6° F.; leucocytes, 10,000. No injection. 11.15 A. M., temperature, 99.6°; leucocytes, 9,375. 2 P. M., temperature, 100°; leucocytes, 11,000. 5 P. M., temperature, 101°; leucocytes, 17,000. No reaction. There was a marked swelling at point of yesterday's injection. This was red and hard and very painful.

December 16th.—The seat of injection is still so swollen and painful that at the patient's wish no injection was given and no blood counts made.

December 17th.—9.15 A. M., temperature, 99.8° F.; leucocytes, 9,687. No injection. 11 A. M., temperature, 99.8°; leucocytes, 8,125. 5 P. M., temperature, 99.8°; leucocytes, 8,750. Feels well.

December 18th.—8.30 A. M., temperature, 99.8° F.; leucocytes, 8,135. No injection. 11 A. M., temperature, 99.8°; leucocytes, 9,375. 1.15 P. M., temperature, 99.8°; leucocytes, 10,000. 3.30 P. M., temperature, 99.8°; leucocytes, 8,125. 5.30 P. M., temperature, 100°; leucocytes, 10,635. The patient felt unusually well during the day and thinks the KOH injections have helped him.

December 19th.—8.15 A. M., temperature, 99.8° F.; leucocytes, 13,125. Twelve cubic centimetres of the nuclein solution given. 9.30 A. M., temperature, 99.8°; leucocytes, 7,500. 12 M., temperature, 99.8°; leucocytes, 8,125. 1.30 P. M., temperature, 99.8°; leucocytes, 9,375. 3.30 P. M., temperature, 100.1°; leucocytes, 13,128. Slight chill. 5.30 P. M., temperature, 100.6°; leucocytes, 15,000. Reaction.

December 20th.—8.30 A. M., temperature, 99.8° F.; leucocytes, 8,125. Fourteen cubic centimetres of the nuclein solution injected. 8.45 A. M., temperature, 98.8°; leucocytes, 8,135. 10 A. M., temperature, 98.8°; leucocytes, 7,500. 11 A. M., temperature, 98.8°; leucocytes, 8,125. 2 P. M., temperature, 99.8°; leucocytes, 8,750. 3.30 P. M., temperature, 99.8°; leucocytes, 11,250. Slight reaction. 5 P. M., temperature, 100.1°; leucocytes, 14,375. Slight reaction.

December 21st.—8.30 A. M., temperature, 100° F.; leucocytes, 10,600. Sixteen cubic centimetres of the nuclein solution injected. 10 A. M., temperature, 99.8°; leucocytes, 8,125. 11.30 A. M., temperature, 99.8°; leucocytes, 14,375. 2 P. M., temperature, 100.1°; leucocytes, 11,250. 3.30 P. M., temperature, 98.8°; leucocytes, 11,250. 5 P. M., temperature, 99.8°; leucocytes, 8,750. No reaction.

December 22d.—9 A. M., temperature, 99.8° F.; leucocytes, 8,750. Ten cubic centimetres of the nuclein solution injected. 10.30 A. M., temperature, 100.4°; leucocytes, 11,250. 11.30 A. M., temperature, 100.4°; leucocytes, 11,250. 1.30 P. M., temperature, 100.4°; leucocytes, 14,375. 3.30 P. M., temperature, 101°; leucocytes, 8,375. No reaction. 5.30 P. M., temperature, 99.8°;

leucocytes, 12,500. These observations were continued until the 26th. The injection of twelve cubic centimetres of the nuclein solution daily produced no reaction. But the daily average of leucocytes was raised to 12,000, instead of the average of 9,000 before the injections were begun. There was no marked increase at any one time, but all of the counts were moderately increased. During the injection of the KOH solution the patient had slight diarrhoea, as did all of the others to whom this was given. This patient thought that the injections, both of KOH and nuclein, gave him increased strength and appetite. The injections were stopped for a week, and the leucocytes fell to the old average of 9,000. Injections of five cubic centimetres of the nuclein were begun and kept up for two months. During this time there was no reaction that could be separated from the symptoms of his disease, and counts of the leucocytes showed no leucocytosis. The patient improved during the first month, but afterward failed rapidly.

CASE XVI.—Mrs. H., a case of chronic bronchitis, referred from the gynaecological clinic for treatment for this condition. She had been under care in that clinic for laceration of the cervix. The patient was in fair condition. Her haemoglobin was 85, the red blood-corpuscles, 4,500,000. Her leucocyte range, counted for three days before beginning the injections, was as follows:

December 23, 1894.—10 A. M., temperature, 98.6° F.; leucocytes, 6,786. 12 M., temperature, 98.6°; leucocytes, 6,875. 2 P. M., temperature, 98.6°; leucocytes, 11,250. 5 P. M., temperature, 98.6°; leucocytes, 10,675.

December 24th.—9 A. M., temperature, 98.6° F.; leucocytes, 9,375. Five cubic centimetres of a 0.26-percent. solution of KOH injected. 10.30 A. M., temperature, 98.6°; leucocytes, 13,135. 2 P. M., temperature, 98.6°; leucocytes, 11,250. 5 P. M., temperature, 98.6°; leucocytes, 8,750. No reaction.

December 25th.—9 A. M., temperature, 98.6° F.; leucocytes, 9,375. Five cubic centimetres of the KOH solu-

tion injected. 11 A. M., temperature, 98.6°; leucocytes, 9,375. 2 P. M., temperature, 98.6°; leucocytes, 10,000. 5 P. M., temperature, 98.6°; leucocytes, 12,500. No reaction.

December 26th.—9 A. M., temperature, 98.6° F.; leucocytes, 8,125. Five cubic centimetres of the KOH solution injected. 11 A. M., temperature, 98.6°; leucocytes, 12,500. 2 P. M., temperature, 98.6°; leucocytes, 15,000. Slight reaction. 5 P. M., temperature, 100.8°; leucocytes, 13,725. Slight reaction.

December 27th.—9 A. M., temperature, 98.6° F.; leucocytes, 11,250. Five cubic centimetres of the KOH solution injected. 11 A. M., temperature, 100°; leucocytes, 12,500. 2 P. M., temperature, 100°; leucocytes, 11,875. Slight reaction. 5 P. M., temperature, 98.8°; leucocytes, 8,750.

December 28th.—9 A. M., temperature, 98.6° F.; leucocytes, 8,750. Five cubic centimetres of the KOH solution injected. 11 A. M., temperature, 98.6°; leucocytes, 9,375. 2 P. M., temperature, 98.6°; leucocytes, 8,750. 5 P. M., temperature, 98.6°; leucocytes, 8,750. No reaction.

December 29th.—9.30 A. M., temperature, 98.6° F.; leucocytes, 9,876. Five cubic centimetres of the nuclein solution injected. 11 A. M., temperature, 100°; leucocytes, 20,000. Reaction. 2 P. M., temperature, 102°; leucocytes, 15,000. Strong reaction. 5 P. M., temperature, 99.8°; leucocytes, 13,750. The patient was very ill all the day with the symptoms common to the reaction obtained in the other cases. The point of injection was very red and painful.

December 30th.—10.30 A. M., temperature, 100° F.; leucocytes, 12,000. Five cubic centimetres of the nuclein solution injected. 12.30 P. M., temperature, 100°; leucocytes, 18,750. 2.30 P. M., temperature, 100°; leucocytes, 13,750. 5 P. M., temperature, 98.8°; leucocytes, 12,500. The patient had the same symptoms as yesterday, but in a less degree. The point of injection was still red and sensitive, but less so than yesterday.

34 EFFECTS OF YEAST NUCLEIN ON LEUCOCYTES.

December 31st.—8.30 A. M., temperature, 98.6° F.; leucocytes, 11,250. Five cubic centimetres of the nuclein solution injected. 12 M., temperature, 98.6°; leucocytes, 8,125. 2 P. M., temperature, 98.6°; leucocytes, 8,125. 5.30 P. M., temperature, 98.6°; leucocytes, 11,500. The patient has been much better all day, and there was much less redness about the points of injection.

January 1, 1895.—Five cubic centimetres of the nuclein were injected, but no counts made.

January 2d.—9 A. M., temperature, 98.6° F.; leucocytes, 9,375. Five cubic centimetres of the nuclein injected. 11.30 A. M., temperature, 98.6°; leucocytes, 7,500. 2 P. M., temperature, 98.6°; leucocytes, 7,500. 5.30 P. M., temperature, 98.6°; leucocytes, 8,750. The patient was well all day and there were no local symptoms.

January 3d.—9.30 A. M., temperature, 98.6° F.; leucocytes, 8,155. Five cubic centimetres of the nuclein solution injected. 12 M., temperature, 98.6°; leucocytes, 10,000. 2 P. M., temperature, 98.6°; leucocytes, 7,000. 5 P. M., temperature, 98.6°; leucocytes, 6,875. No reaction.

January 4th.—9 A. M., temperature, 98.6° F.; leucocytes, 8,750. Five cubic centimetres of the nuclein injected. 11.30 A. M., temperature, 98.6°; leucocytes, 10,000. 2.30 P. M., temperature, 98.6°; leucocytes, 10,000. No reaction. 7.30 P. M., temperature, 98.6°; leucocytes, 8,750.

January 5th.—11 A. M., temperature, 98.6° F.; leucocytes, 7,500. Five cubic centimetres of the nuclein solution injected. 2 P. M., temperature, 98.6°; leucocytes, 11,250. 8 P. M., temperature, 98.8°; leucocytes, 13,000. Slight reaction.

January 6th.—Five cubic centimetres of the nuclein injected. No count. No reaction.

January 7th.—9 A. M., temperature, 98.6° F.; leucocytes, 7,500. Five cubic centimetres of the nuclein injected. 11.30 A. M., temperature, 98.6°; leucocytes,

10,000. 5 P. M., temperature, 98.6°; leucocytes, 10,000. No reaction.

January 8th.—8.30 A. M., temperature, 98.6° F.; leucocytes, 13,725. Five cubic centimetres of the nuclein injected. 11.30 A. M., temperature, 98.6°; leucocytes, 8,750. 1.30 P. M., temperature, 98.6°; leucocytes, 10,000. 5 P. M., temperature, 98.6°; leucocytes, 10,000. No reaction.

January 10th.—8.45 A. M., temperature, 98.8° F.; leucocytes, 13,275. Eight cubic centimetres of the nuclein injected in two portions into the right gluteal. 12.15 P. M., temperature, 101°; leucocytes, 16,875. Hard chill. 1.30 P. M., temperature, 101°; leucocytes, 16,875. Severe reaction. 5 P. M., temperature, 102°; leucocytes, 15,625. Severe reaction.

January 11th.—9 A. M., temperature, 99.4° F.; leucocytes, 20,000. The patient was so ill that she wished the injection and blood count discontinued for this day.

January 12th.—11 A. M., temperature, 99.4° F.; leucocytes, 15,000. 1.30 P. M., temperature, 101°; leucocytes, 15,000. The reaction continued and was very severe. The right gluteal was very red, indurated, and sensitive. No injection given.

January 13th.—8.30 A. M., temperature, 101° F.; leucocytes, 22,800. 11 A. M., temperature, 101°; leucocytes, 25,000. The local reaction has increased, the right buttock being covered with a bright-red flush; the point of injection was red and much indurated. No injection was given. 1.30 P. M., temperature, 101.8°; leucocytes, 23,000. From finger. 1.30 P. M., temperature, 101.8°; leucocytes, 26,000. From gluteal. The patient compared the symptoms to those of *grippe*.

January 14th.—11.30 A. M., temperature, 101.1° F.; leucocytes, 20,000. From finger. 11.30, temperature, 101.1°; leucocytes, 27,000. From gluteal. The patient felt much worse to-day. The seat of the double injection of the 10th was very red and elevated; slight fluctuation was obtained. The temperature rose to 103° F. in the afternoon, the leucocytes to 30,000.

An incision was made, and about two ounces of oily serum withdrawn. This consisted almost wholly of fat globules, numerous leucocytes, and red blood-corpuscles. A bacteriological examination of this was negative.

The patient decided to give up the treatment, so no more injections were given and no more counts made. The abscess was healed in a few days and the patient felt well. During the treatment she gained ten pounds, but the bronchitis remained as before.

CASE XVII.—Miss T., aged twenty-five, was under treatment for nervous dyspepsia. The patient was in fair condition. Haemoglobin, 90; red blood-corpuscles, 4,500,000; leucocytes, 5,000 to 8,000. These were counted for three days before beginning the injections. The lowest count during this time was 5,625, the highest was 8,750.

December 17, 1894.—10 A. M., temperature, 98.6° F.; leucocytes, 5,625. 11.25 A. M., temperature, 98.6°; leucocytes, 5,625. 1.30 P. M., temperature, 98.6°; leucocytes, 8,750. 3.30 P. M., temperature, 98.6°; leucocytes, 8,750. 5 P. M., temperature, 98.8°; leucocytes, 8,750.

December 18th.—9.25 A. M., temperature, 98.6° F.; leucocytes, 6,875. Sixteen cubic centimetres of a 0.26-per-cent. solution of NaOH injected. 10 A. M., temperature, 98.6°; leucocytes, 5,000. 12 M., temperature, 98.6°; leucocytes, 4,000. 1.15 P. M., temperature, 98.6°; leucocytes, 8,750. 3 P. M., temperature, 98.6°; leucocytes, 8,750. 5.30 P. M., temperature, 98.8°; leucocytes, 8,750. No reaction.

December 19th.—9 A. M., temperature, 98.6° F.; leucocytes, 5,625. Fourteen cubic centimetres of the 0.26-per-cent. solution of KOH injected. 9.15 A. M., temperature, 98.6°; leucocytes, 3,750. 10.30 A. M., temperature, 98.6°; leucocytes, 10,000. 11.30 A. M., temperature, 98.6°; leucocytes, 9,375. 2 P. M., temperature, 99.8°; leucocytes, 12,500. Headache. 3.30 P. M., temperature, 100°; leucocytes, 11,875. 5.15 P. M., temperature, 100°; leucocytes, 8,750. Slight reaction.

December 20th.—The patient was ill all the night with a severe reaction, nausea, headache, pain in bones, chilly sensations, and fever. 8.30 A. M., temperature, 101° F.; leucocytes, 16,000. No injection. Point of injection in gluteal very red. 11 A. M., temperature, 101.8°; leucocytes, 16,876. 2 P. M., temperature, 103°; leucocytes, 17,000. Severe reaction. 5 P. M., temperature, 104°; leucocytes, 17,000. The patient compared the reaction to the *grippe*.

December 21st.—The reaction continued all night, though the patient felt better this morning. The point of the KOH injection in the gluteal was swollen over an area as large as a hand, very red, hard, and sensitive. 9.45 A. M., temperature, 99.8° F.; leucocytes, 23,125. 10 A. M., temperature, 99.8°; leucocytes, 23,700. Sixteen cubic centimetres of the KOH injected into the other gluteal (left). 10.15 A. M., temperature, 99.9°; leucocytes, 18,125. 11.15 A. M., temperature, 99.9°; leucocytes, 16,875. 2 P. M., temperature, 100.2°; leucocytes, 22,500. 3.30 P. M., temperature, 102°; leucocytes, 18,125. 5.30 P. M., temperature, 101°; leucocytes, 12,500. Reaction all day.

December 22d.—The reaction continued, but of less degree. The gluteals were red and swollen. No injection was given on this day. 9.30 A. M., temperature, 99.8° F.; leucocytes, 20,000. 11 A. M., temperature, 99.8°; leucocytes, 10,625. 3.30 P. M., temperature, 99.8°; leucocytes, 6,875. Much better. 5 P. M., temperature, 99°; leucocytes, 6,875. Much better.

December 23d.—The patient felt well this morning. There were still redness and swelling at the point of injection in both gluteals, but they were much less sensitive. No injection and no reaction. 10.30 A. M., temperature, 98.6° F.; leucocytes, 8,000. 10.45 A. M., temperature, 98.6°; leucocytes, 5,625. 11.30 A. M., temperature, 98.6°; leucocytes, 6,250. 2 P. M., temperature, 98.6°; leucocytes, 8,125. 5 P. M., temperature, 98.6°; leucocytes, 8,750.

December 24th.—8.30 A. M., temperature, 98.6° F.;

leucocytes, 7,876. 11.30 A. M., temperature, 98.6°; leucocytes, 6,250. 2 P. M., temperature, 98.6°; leucocytes, 8,125. 5 P. M., temperature, 98.6°; leucocytes, 8,750. No injection on this day. The patient had entirely recovered; the local condition was much improved. The red flush had disappeared.

December 25th.—8.30 A. M., temperature, 98.6° F.; leucocytes, 8,000. Five cubic centimetres of the nuclein solution were injected. 11.30 A. M., temperature, 98.6°; leucocytes, 6,875. 2 P. M., temperature, 100°; leucocytes, 11,250. Slight reaction. 4.45 P. M., temperature, 100.4°; leucocytes, 14,375. Slight reaction.

December 26th.—9.30 A. M., temperature, 100° F.; leucocytes, 9,375. Five cubic centimetres of the nuclein solution injected. 11 A. M., temperature, 98.9°; leucocytes, 10,000. 2 P. M., temperature, 100.4°; leucocytes, 12,500. Slight reaction. 5 P. M., temperature, 100.4°; leucocytes, 10,000. Slight reaction. The patient complained of much pain at the points of injection.

December 27th.—9 A. M., temperature, 98.6° F.; leucocytes, 10,000. Five cubic centimetres of the nuclein injected. 11 A. M., temperature, 98.6°; leucocytes, 9,375. 2.30 P. M., temperature, 98.6°; leucocytes, 11,375. 5 P. M., temperature, 98.6°; leucocytes, 10,625. No reaction.

December 28th.—10 A. M., temperature, 98.6° F.; leucocytes, 12,250. Five cubic centimetres of nuclein injected. 11.15 A. M., temperature, 98.8°; leucocytes, 11,250. 2 P. M., temperature, 98.8°; leucocytes, 12,500. 5 P. M., temperature, 98.8°; leucocytes, 10,000. No reaction.

December 29th.—9.30 A. M., temperature, 98.6° F.; leucocytes, 6,250. Five cubic centimetres of the nuclein injected. 11.30 A. M., temperature, 98.6°; leucocytes, 13,250. Chill. 2 P. M., temperature, 100°; leucocytes, 10,000. Slight reaction. 5.30 P. M., temperature, 100°; leucocytes, 12,250. The point of injection was very painful, but not much inflamed.

December 30th.—10 A. M., temperature, 98.6° F.; leu-

cocytes, 13,125. Five cubic centimetres of the nuclein solution injected. 12 M., temperature, 98.6°; leucocytes, 9,275. 2 P. M., temperature, 98.6°; leucocytes, 7,500. 5.30 P. M., temperature, 98.6°; leucocytes, 8,750. No reaction.

December 31st.—9 A. M., temperature, 99.8° F.; leucocytes, 17,500. Five cubic centimetres of the nuclein solution injected. 11.30 A. M., temperature, 99.8°; leucocytes, 12,750. Moderate reaction. 2 P. M., temperature, 100°; leucocytes, 15,000. Moderate reaction. 5.30 P. M., temperature, 100.1°; leucocytes, 15,000. Moderate reaction.

January 1, 1895.—Five cubic centimetres of nuclein injected. No count. Slight reaction.

January 2d.—9.30 A. M., temperature, 98.6° F.; leucocytes, 7,500. No injection. 11.30 A. M., temperature, 98.6°; leucocytes, 7,500. 2.30 P. M., temperature, 98.6°; leucocytes, 6,250. 5 P. M., temperature, 98.6°; leucocytes, 9,375. No symptoms.

January 3d.—9 A. M., temperature, 98.6° F.; leucocytes, 7,875. Five cubic centimetres of nuclein injected. 12 M., temperature, 98.6°; leucocytes, 10,000. 2 P. M., temperature, 98.6°; leucocytes, 13,000. Slight reaction. 5.30 P. M., temperature, 98.6°; leucocytes, 13,000.

January 4th.—9 A. M., temperature, 98.6° F.; leucocytes, 9,375. Five cubic centimetres of nuclein injected. 11.30 A. M., temperature, 98.6°; leucocytes, 10,350. 2.30 P. M., temperature, 98.6°; leucocytes, 9,375. No reaction. 7.30 P. M., temperature, 99.8°; leucocytes, 10,000. No reaction.

January 5th.—11 A. M., temperature, 98.6° F.; leucocytes, 7,500. Five cubic centimetres of nuclein injected. 2 P. M., temperature, 98.6°; leucocytes, 13,125. No reaction. 6 P. M., temperature, 99.8°; leucocytes, 8,125. No reaction.

January 6th.—9 A. M., leucocytes, 8,760. 11 A. M., sixteen cubic centimetres of nuclein injected. 11.30 A. M., temperature, 98.6° F.; leucocytes, 9,687. 2 P. M.,

temperature, 101°; leucocytes, 16,000. Reaction. 3 P. M., temperature, 102°; leucocytes, 17,250. Chill. 5 P. M., temperature, 104°; leucocytes, 22,000. Strong reaction. The patient declined to receive any more injections, so further investigation was stopped.

CASE XVIII.—Mr. C., student, in good health. Leucocyte average 8,000. Five cubic centimetres of the nuclein were taken by the mouth for three weeks. He had no reaction, and there was no disturbance of the leucocytes.

CASE XIX.—Mr. N., patient in the surgical clinic for fistula, was given five cubic centimetres of nuclein daily for six weeks without reaction or disturbance of the leucocytes.

CASE XX.—Mrs. H., aged forty-five years, under treatment for chronic bronchitis, took five cubic centimetres of the nuclein solution three times daily for two months. The daily range of leucocytes remained as before the drug was taken. The average stood at 7,500, with very slight variation. There was no reaction. The patient professed to be benefited by the treatment.

CASE XXI.—Miss T., aged eighteen years, under treatment for tuberculosis of the femur, took five cubic centimetres of the nuclein solution for six weeks three times daily without reaction. Leucocyte counts made at frequent but irregular intervals showed no leucocytosis.

CASE XXII.—Mr. F., aged twenty-five years, pulmonary tuberculosis, with a constant leucocytosis of 15,000 to 20,000, took five cubic centimetres of the nuclein solution by the mouth daily for three weeks without reaction or change in the leucocyte range. No change in the patient's condition.

CASE XXIII.—Mr. R., aged twenty-six years, student, in good health, took five cubic centimetres of the nuclein solution by the mouth three times daily for three weeks. No effect was observed, and no disturbance of the leucocytes.

CASE XXIV.—Mr. S., aged twenty-two years, under treatment for secondary anaemia following haemorrhage, was given five cubic centimetres of the nuclein solution by the mouth three times daily for three months without reaction or disturbance of the leucocyte range. For one month he took in the same manner eight cubic centimetres of an extract of bone marrow. This gave no reaction, and the leucocytes counted at frequent intervals showed always a very low count, never rising above 6,000. In addition to the marrow extract the patient had a diet during this month consisting almost entirely of cooked marrow and blood-puddings. During this month he made a gain of twenty per cent. haemoglobin. It is, of course, an open question as to what part the treatment had in bringing about this improvement.

CASE XXV.—Mr. S., aged forty-five years, with genito-urinary tuberculosis, took five cubic centimetres of the nuclein solution by the mouth three times daily for six weeks under observation without reaction or leucocytosis. For three weeks he had daily injections of the same amount without reaction or change in the leucocyte count. There was no improvement under the treatment.

CASE XXVI.—Dr. R., with genito-urinary tuberculosis, had received daily injections of five cubic centimetres of nuclein solution for three months without interruption. He had rarely any reaction. According to his statement, the reaction seemed to depend upon the manner in which the injection was given. He was under observation for several days only when his leucocytes were counted. For two days the count was as follows: 9 A. M., leucocytes, 5,625. 11.15 A. M., leucocytes, 6,875. 2.45 P. M., leucocytes, 9,375. 5 P. M., leucocytes, 7,500. Though this observation was very short and incomplete, it would go to show that there had been no lasting leucocytosis produced by the long-continued use of the nuclein injection. Under this treatment the patient's symptoms disappeared, and pus and tuber-

cle bacilli were no longer found in his urine. (This patient was under Dr. Vaughan's treatment, and was seen by me for a few days only when the leucocytes were counted.)

In summing up the results of the experiments with these twenty-six cases we find—

1. In eight cases in which five cubic centimetres of the nuclein solution were given by the mouth three times daily for different periods of time there was no reaction and no disturbance of the leucocyte range. In one case in which there was given a glycerin extract of bone marrow for a month there was practically a hypoleucocytosis. These cases were Case XVIII, normal individual; Case XIX, rectal fistula (tuberculous?); Case XX, chronic bronchitis; Case XXI, bone tuberculosis; Case XXII, pulmonary tuberculosis with leucocytosis; Case XXIII, normal individual; Case XXIV, secondary anaemia; Case XXV, genito-urinary tuberculosis.

2. In nine cases in which injections of five cubic centimetres of the nuclein were given daily for different periods of time there was no reaction and no leucocytosis. These cases were Case XXVI, genito-urinary tuberculosis; Case XIII, sexual neurasthenia (on one day there was a slight reaction and the daily average was increased); Case XI, pulmonary tuberculosis with leucocytosis; Case X, pulmonary tuberculosis without leucocytosis; Case IX, tuberculosis of cervical glands; Case IV, bone tuberculosis with leucocytosis; Case V, pulmonary tuberculosis; Case VI, pulmonary tuberculosis; Case VII, bone tuberculosis; Case VIII, genito-urinary tuberculosis; Case XV, pulmonary tuberculosis. (The injection of five cubic centimetres daily for two months

in this case had no effect, but reaction and leucocytosis were produced by larger doses.)

3. In eight cases injections of nuclein in amounts from four to sixteen cubic centimetres produced a definite reaction and well-marked leucocytosis. These cases were Case I, sexual neurasthenia; Case II, nervous dyspepsia; Case III, bone tuberculosis with leucocytosis; Case XII, chronic furunculosis of skin (one slight reaction with leucocytosis); Case XIV, muscular rheumatism; Case XVI, chronic bronchitis; Case XVII, nervous dyspepsia; Case XV, pulmonary tuberculosis.

4. The leucocytosis occurred only when there was a local and general reaction. It occurred more constantly when a large injection was given. The occurrence of reaction and leucocytosis after the injections was not constant in any of the cases, but subject to wide variations. The reaction appeared sometimes very soon, at other times it was delayed. The local reaction consisted of a swelling and induration of the area about the point of injection, usually about the size of a hand and covered with a deep red flush. The general symptoms were compared by the patients to *grippe*, and consisted of headache, nausea, vomiting, weakness, pain in muscles and bones, chills, and fever. Epistaxis and diarrhoea were also prominent symptoms. As a rule, the reaction lasted but a few hours, but on several occasions it extended over two or three days, the leucocytosis continuing during this time. The leucocytosis usually reached its height just before the highest temperature, but declined much more slowly. In some instances the leucocytosis occurred without any increase of temperature.

5. Injections of a 0.6-per-cent. NaCl solution and

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of a 0.26-per-cent. solution of NaOH produced no reaction and no leucocytosis. The injection of a 0.26-per-cent. solution of KOH produced a reaction and a leucocytosis in all respects similar to that resulting from the injections of the nuclein solution, except that these followed the nuclein injections much more uniformly than they did the injection of the alkali.

6. When the counts were made soon after giving the injection, it was found that there was almost always a marked decrease in the number of the leucocytes. This lasted usually two to three hours, after which the increase took place. This point has been noted by many observers who have tried the effect of other injections upon the leucocytes.

7. It might be questioned whether the leucocytosis produced by injections is not wholly the result of an inflammatory process. I have found that the application of a cantharides plaster an inch wide by four long to the lumbar region of a healthy individual increased the leucocytes in six hours to three times the normal number. The injection of large amounts of solutions in themselves not inert may be sufficient to produce a general leucocytosis because of the local damage to the tissues. But many things make it doubtful that this is an inflammatory leucocytosis. The fact that the general average of the leucocytes is raised at times when there is no local reaction is very much opposed to this idea.

8. The proportional count of the white cells in those cases in which a leucocytosis occurred remained practically unchanged, except in a few cases in which the percentage of the polynuclear forms was increased.

Therefore, in conclusion, I should say that the

power of nuclein to increase the leucocytes can only be definitely known when the nuclein is injected in solutions that in themselves produce no leucocytosis. Systematic observations of the effect of the administration of pure nucleinic acid are now being carried on in this laboratory by a colleague, who will later make report of the same. Moreover, since large injections produced invariably some degree of leucocytosis, experiments must be made with doses of greater strength. Dr. Vaughan informs me that the solution used was really less than a one-half-per-cent. solution, and that at present he is using a ten-per-cent. solution. The effect of this stronger solution will be studied and reported later.

NOTE.—Since the writing of this article Dr. Vaughan has published, in the *Medical News* for February 27 to March 27, 1897, reports of cases in which pure solutions of much greater strength were used with more constant effects upon the leucocytes. This report is therefore valuable as it shows the results obtained by very weak solutions, and, moreover, presents systematic leucocyte counts made upon various individuals for continued periods of time. It is hoped that attention may be called to the importance of this procedure.

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